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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/277,575	03/27/1999	MARTHA KAREN NEWELL	V00139/70028	3748

7590 07/17/2006

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/277,575	**Applicant(s)** NEWELL, MARTHA KAREN	
	Examiner F. Pierre VanderVegt	**Art Unit** 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 June 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because: Applicant argues that the specification is fully enabling for the claimed invention and that the Examiner has failed to make a prima facie case for a lack thereof. Applicant asserts that the Examiner has misunderstood Applicant's previous arguments. The Examiner disagrees with both statements. The claims are drawn to a method of treatment. While, as asserted by Applicant, not all claims are drawn to the treatment of a tumor, all claims are drawn to an in vivo treatment method wherein MHC class II expression is induced or increased upon the cell. The treatment then further calls for attacking the cell expressing MHC class II with an MHC class II ligand in order to "decrease mitochondrial potential" or cause lysis of the target cell. The claimed method is not drawn simply to the upregulation of MHC class II expression on cells which either do or don't constitutively express MHC class II on their surface, rather the method includes a further step of eliminating the MHC class II cells. it has not been questioned by the Examiner as to whether appicant could up-regulate MHC class II expression on the cells, rather the lack of enablement comes into play in regard to the ability to target a desired population of cells for elimination, or "reduction of mitochondrial membrane potential," with a second agent that is an MHC class II ligand. the MHC class II ligand will bind to all MHC class II expressing cells with equal affinity and reduce mitochondrial membrane potential or lysis of the cells. Irrespective of whether the expression on MHC class II on a given cell is naturally occurring, such as an antigen presenting cell, or induced by Applicant's first step of the claimed method, such as on a tumor cell [claim 39] or a "mammalian cell which is not an antigen presenting cell" [claim 13], the MHC class II haplotype expressed on all cells in the body of the subject being treated will be of the same haplotype. Applicant's method does not cause the expression of a haplotype on target cells that is different than that expressed by antigen presenting cells. Accordingly, Applicant's method will equally lyse or decrease mitochondrial membrane potential on the induced cells and natural antigen presenting cells. the claimed method is not enabled by the specification because Applicant has no way of differentiating between antigen presenting cells and the desired target cells in the second, lysis or decreasing mitochndrial membrane potential, step. Applicant's reliance upon ADRIAMYCIN as the agent that reduces mitochondrial membrane potential as being an example enabling Applicant's broad recitation is not credible. The properties of ADRIAMYCIN were discussed in the previous Office Action. ADRIAMYCIN interchelates DNA in actively dividing cells, such as tumor cells. However, this characteristic does not describe the vast majority of mature antigen presenting cells which express MHC class II. The "class of molecules" Applicant is attempting to represent using ADRIAMYCIN to demonstrate functionality or safety of the class is much broader than just DNA intercalating agents, so it is unclear how ADRIAMYCIN can be considered representative of the class. Applicant refers to the MPEP regarding the applicability of a model to a specific condition. However it is noted that all of Applicant's examples from the specification are in vitro examples carried out in isolated cells. The claimed invention, however, encompasses and recites in vivo treatment of a subject. The specification is not enabling for such an in vivo treatment because there is no evidence that the claimed method would be able to affect the recited target cells of the method in a whole body system context.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
July 11, 2006

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644